

SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. GENERAL INFORMATION

Device Generic Name: Stent, Coronary

Device Trade Name: PRO-Kinetic Energy Cobalt Chromium (CoCr) Coronary Stent System

Device Procode: MAF

Applicant's Name and Address: BIOTRONIK, Inc.
6024 Jean Road
Lake Oswego, OR 97035

Date(s) of Panel Recommendation: None

Premarket Approval Application (PMA) Number: P160003

Date of FDA Notice of Approval: February 14, 2017

II. INDICATIONS FOR USE

The PRO-Kinetic Energy Cobalt Chromium (CoCr) Coronary Stent System is indicated for improving coronary luminal diameter in patients with de novo or restenotic lesions in native coronary arteries with a reference vessel diameter ranging from 2.25 mm to 4.0 mm and lesion length $\leq$ 31 mm.

III. CONTRAINDICATIONS

Contraindications for the PRO-Kinetic Energy Cobalt Chromium (CoCr) Coronary Stent System include, but are not limited to:

- Patients with a known hypersensitivity or allergy to stent coating materials (amorphous silicon carbide) or to L-605 CoCr alloy (cobalt, chromium, tungsten, nickel).
- Patients with a known severe reaction to contrast agents who cannot be adequately pre-medicated prior to the stent placement procedure.

Coronary artery stenting is contraindicated for use in the following:

- Patients who are contraindicated for antiplatelet and/or anticoagulation therapy.
- Patients who are judged to have a lesion that prevents complete inflation of an angioplasty balloon.

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the PRO-Kinetic Energy Cobalt Chromium (CoCr) Coronary Stent System labeling.

V. DEVICE DESCRIPTION

The PRO-Kinetic Energy Cobalt Chromium (CoCr) Coronary Stent System consists of a balloon-expandable stent (1) pre-mounted on a fast-exchange delivery system. The stent is intended as a permanent implant. It is made from a cobalt chromium alloy (L-605) and is coated with a thin layer of amorphous silicon carbide (proBIO).

There are two different stent designs: small (2.25 – 3.0 mm diameter) and medium (3.5 – 4.0 mm diameter). See **Table 1** below. The delivery system is a fast-exchange percutaneous transluminal coronary angioplasty (PTCA) catheter with a working length of 140 cm. To facilitate fluoroscopic visualization and positioning, the stent is centered between two radiopaque markers (2a and 2b). The proximal shaft of the stent system is a hypotube (3). It has a single Luer port (4) for connecting an inflation/deflation device to inflate/deflate the balloon (5). The catheter has a hydrophobic coating on the outer surface of the proximal shaft and a hydrophilic coating on the outer surface of the distal shaft. The guide wire lumen (6) starts at the delivery system tip (7) and ends at the guide wire exit point (8), 29 cm from the distal end. The stent system is compatible with guidewires (9) of 0.014" (0.36 mm) diameter and guiding catheters with an inner diameter of ≥ 0.056 " (1.42 mm). To indicate when the delivery system tip exits from the guiding catheter, shaft exit markers are located on the hypotube 92 cm (10a) (brachial technique) and 102 cm (10b) (femoral technique) from the distal end of the delivery system. To facilitate handling of the stent system, the hub (11) has a "click-in" hypotube fastener (12) that should be used when the stent system is stored on the preparation table.

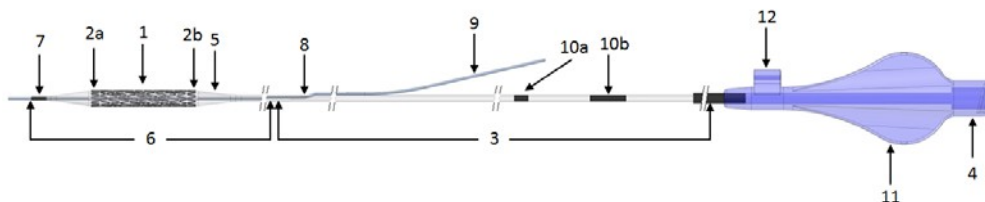


Table 1: Stent Parameters

	Stent Inner Diameter [mm]					
Stent design	SMALL				MEDIUM	
Nominal strut thickness	60µm				80µm	
Percent stent free area	82%	84%	86%	87%	88%	89%
Stent length [mm]	2.25	2.50	2.75	3.0	3.5	4.0
9	x	x	x	x	x	x
13	x	x	x	x	x	x
15	x	x	x	x	x	x
18	x	x	x	x	x	x
20	x	x	x	x	x	x
22		x	x	x	x	x
26			x	x	x	x
30			x	x	x	x
35					x	x
Nominal distance between radiopaque marker and stent	0.3 mm					
Maximum expandable diameter*	3.50 mm			4.65 mm		
*If post-dilation is required, DO NOT post-dilate the stent more than the maximum expandable diameter.						

VI. ALTERNATIVE PRACTICES AND PROCEDURES

There are several other alternatives for the treatment of coronary artery disease which may include: exercise, diet, smoking cessation, drug therapy, percutaneous coronary interventions (such as angioplasty and placement of bare metal stents, drug eluting stents, etc.), and coronary artery bypass graft surgery (CABG). Each alternative has its own advantages and disadvantages. A patient should fully discuss available alternatives with his/her physician to determine which method(s) are appropriate to best meet their clinical needs and lifestyle.

VII. MARKETING HISTORY

The PRO-Kinetic Energy Cobalt Chromium (CoCr) Coronary Stent System has been marketed outside the United States (OUS) since 2008; in this period more than 637,000 devices have been sold worldwide. The device has not been withdrawn from marketing for any reason related to its safety or effectiveness. A list of countries where the PKE Stent System is distributed is provided in **Table 2**.

Table 2: List of Countries Where PKE Stent System is Distributed

Argentina	Canada	Finland	Israel	Malta	Romania	Sweden
Armenia	Chile	France	Italy	Mexico	Russia	Switzerland
Australia	China	Georgia	Jordan	Montenegro	Saudi Arabia	Thailand
Austria	Colombia	Germany	Kazakhstan	Myanmar	Serbia	Turkey
Bahrain	Croatia	Guatemala	Kuwait	Netherlands	Singapore	U.A.E
Bangladesh	Curacao	Hong Kong	Latvia	Palestine	Slovakia	U.K.
Belgium	Cyprus	Hungary	Lebanon	Panama	Slovenia	Venezuela
Bosnia-Herz.	Czech. Rep.	India	Lithuania	Paraguay	South Africa	Vietnam
Brazil	Denmark	Indonesia	Macedonia	Poland	South Korea	Yemen
Bulgaria	Egypt	Iran	Malaysia	Portugal	Spain	

VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

Below is a list of the potential adverse effects (e.g., complications) associated with the use of the PKE Stent System:

- Allergic reactions to contrast media, antiplatelet aggregation or anticoagulant medications, amorphous silicon carbide and / or L-605 CoCr (cobalt, chromium, tungsten and nickel)
- Arrhythmic events: Ventricular tachycardia, ventricular fibrillation, atrial fibrillation, bradycardia
- Bleeding events: Access site bleeding or hemorrhage, hemorrhage requiring transfusion or other treatment
- Cardiac events: Myocardial infarction or ischemia, abrupt closure of coronary artery, restenosis of treated artery, cardiogenic shock, angina, tamponade, perforation or dissection of coronary artery or aorta, cardiac perforation, need for emergency cardiac surgery, pericardial effusion, aneurysm formation, cardiomyopathy
- Death
- Infection and sepsis
- Neurologic events: Permanent (stroke) or reversible (TIA) neurologic event, femoral nerve injury, peripheral nerve injury
- Renal events: renal insufficiency / renal failure
- Respiratory events: Acute pulmonary edema, congestive heart failure, respiratory insufficiency or failure
- Stent system events: Failure to deliver stent to intended site, stent dislodgement from the delivery system, stent misplacement, stent deformation, stent embolization, stent thrombosis or occlusion, stent fracture, stent migration, inadequate apposition or compression of stent/s, inflation difficulties, rupture or pinhole of the delivery system balloon, deflation difficulties, withdrawal difficulties, embolization of balloon catheter material

- Vascular events: Access site hematoma, hypotension / hypertension, pseudoaneurysm, arteriovenous fistula formation, retroperitoneal hematoma, vessel dissection or perforation, restenosis, thrombosis or occlusion, compromise of side branch patency, vasospasm, peripheral ischemia, dissection, distal embolization (air, tissue, debris, thrombus)

For the specific adverse events that occurred in the Clinical Study, please see Section X below.

IX. SUMMARY OF NONCLINICAL STUDIES

A. IN VITRO BENCH TESTING

In vitro bench testing was performed to assess the functional characteristics of the PKE Stent System. Testing was conducted according to the guidelines provided in *FDA Guidance for Industry and FDA Staff-Non-clinical Tests and Recommended Labeling for Intravascular Stents and Associated Delivery Systems* (April 18, 2010).

Table 3 below summarizes the bench testing performed on the PKE Stent System. The test results are supportive of the device safety and effectiveness.

Table 3: Non-Clinical Engineering Tests of PKE Stent and Delivery System

Test	Test Purpose	Results
Stent Dimensional and Functional Testing		
Identification of Stent Materials	To identify and list all materials used in the construction of the stent body.	Pass
Identification of Stent Coating Materials	To identify and list all materials used for the a-SiC:H coating.	Pass
Surface Characterization	Characterization of the stent surface and a-SiC:H coating.	Elemental components of the coating and stent were characterized and the coating was determined to be acceptably uniform.
Pitting and Crevice Corrosion Resistance – Pre-Fatigue After Simulated Use	To evaluate the susceptibility of the metallic components of the stent to pitting and crevice corrosion after simulated use testing.	Pass

Test	Test Purpose	Results
Accelerated Durability Testing: Stent Overlapped/ Coating Durability/ Fretting Corrosion Assessment	To evaluate the aspects of the long-term integrity of the stent and any coating under cyclic radial loading conditions in overlapping and statically bent configuration and the susceptibility of the metallic components of the stent to fretting corrosion in a simulated physiological environment.	Pass
Galvanic Corrosion	To determine the susceptibility of the metallic components of the stent to Galvanic Corrosion in a simulated physiological environment.	Pass
Dimensional Verification	To inspect and measure the stent body dimensions before placement onto delivery system.	Pass
Percent Surface Area	To determine the surface coverage (stent-artery ratio) of the stent in the vessel. The calculation has been performed for all stent sizes.	Pass
Foreshortening	To determine the foreshortening of the stent.	Pass
Elastic Recoil	To determine the amount of elastic recoil (percent recoil) after deployment to determine the diameter of the stent in its deployed state.	Pass
Stent Integrity	To determine the ability of the stent surface/coating to resist damage due to loading, tracking, and deployment.	Pass
Longitudinal Deformation	To determine the resistance of the stent longitudinal deformations (axial compressions)	For Characterization Only

Test	Test Purpose	Results
Radial Stiffness and Radial Strength	To determine the load/deformation characteristics of the stent during application of a radial load.	Stent revealed acceptable results for radial strength and radial stiffness under simulated clinical loads.
Acute Particulate Evaluation	The purpose of this test is to determine the size and quantity of particles that could be potentially introduced into the bloodstream during delivery, deployment and retraction and to inspect the stent and coating after expansion.	Particulate results were characterized and determined to be at an acceptable level.
Chronic Particulate Evaluation	To investigate the size and quantity of particles under cyclic radial loading conditions in overlapped and statically bent configuration representing an equivalent of 10 years of implantation life.	Particulate results were characterized and determined to be at an acceptable level.
Mechanical Properties of the Stent: Raw Materials and Post-Processing	To determine the mechanical properties of the materials of the stent.	Pass
Stress Analysis / Fatigue Analysis	To determine the stent durability due to worst case physiological loads by means of a Finite Element Analysis and calculation of a Safety Factor (SF).	Pass
Stress Analysis / Fatigue analysis: Overlapped	To determine the stent durability due to worst case physiological loads and configuration by means of a Finite Element Analysis and calculation of a Safety Factor (SF).	Pass
MRI Safety and Compatibility	To determine the effect of Magnetic Resonance on the position and temperature of the PKE Stent. Also to determine the extent of image artifact during MRI.	Pass

Test	Test Purpose	Results
Radiopacity (X-Ray Visibility)	To determine the ability to visualize the stent system and/or stent using the imaging techniques specified in the IFU.	Pass
Delivery System Dimensional and Functional Testing		
Identification of Delivery System Materials	To identify and list all components and their respective materials used in the construction of the delivery system.	Pass
Identification of Packaging Materials	To identify the design and all materials used for the packaging design.	Pass
Dimensional and Visual Inspection	To inspect the physical and dimensional properties of the PKE Stent System.	Pass
Crossing Profile	To measure the crossing profile of the Stent System.	Pass
Dimensional Verification: Shaft Inner and Outer Diameter	To determine the shaft inner and outer diameter.	Pass
Delivery, Deployment, and Retraction (Simulated Use)	To evaluate the performance of the stent and delivery system in reliably delivering the stent to the intended anatomy under simulated clinical conditions.	Pass
Balloon Rated Burst Pressure (RBP)	To determine the rated burst pressure (RBP) of the balloon when deploying the stent.	Pass
Balloon Fatigue	To determine the ability of the balloon to withstand repeated inflation/deflation cycles.	Pass
Balloon Compliance	To determine the relationship between the stent diameter and the balloon inflation pressure.	Pass
Balloon Inflation and Deflation Time	To determine the balloon inflation and deflation time.	Pass
Tensile Strength: Catheter	To determine the bond strength of the joints and/or fixed connections.	Pass

Test	Test Purpose	Results
Tensile Strength: Tip Pull	To determine the bond strength of the joint(s) and/or fixed connections in the distal tip of the delivery system.	Pass
Flexibility and Kink	To evaluate the flexibility and kink resistance of the delivery system.	Pass
Adhesive Strength of Catheter Coating (Coating Integrity)	To evaluate the adhesive strength of the surface coating on the proximal outer shaft of the catheter.	Pass
Coating Integrity	To evaluate the ability of the delivery system coating to resist damage due to loading, tracking, deployment and delivery system withdrawal.	Pass
Particulate Evaluation – Delivery System	To investigate the size and quantity of particles that could potentially be introduced into the blood stream during delivery, deployment and retraction.	Particulate results were characterized and determined to be at an acceptable level.
Stent Securement for Unsheathed Stents	To determine the force that will dislodge the stent from the delivery system after conditioning.	Pass

B. Biocompatibility

As per ISO 10993, the PKE Stent was subjected to the biocompatibility tests identified in Table 4. The PKE delivery system was subjected to the biocompatibility tests identified in Table 5.

Table 4: Stent Biocompatibility Testing

Test Performed	Test Purpose	Results
Cytotoxicity	To determine potential for cytotoxicity of the test article extract	Pass
Sensitization (Magnusson/Kligman)	To evaluate the allergenic potential or potential for sensitization of the test article extracts	Pass
Irritation/Intracutaneous Reactivity	To screen test article extracts for potential to produce irritation	Pass
Acute Systemic Toxicity	To screen test article extracts for potential systemic toxic effects	Pass

Test Performed	Test Purpose	Results
Pyrogenicity	To evaluate the potential of the test article extract to produce a pyrogenic response	Pass
Implantation (14 days)	To determine the potential of the test article to cause local effects	Pass
Implantation (90 days)	To determine the potential of the test article to cause local effects	Pass
Implantation (180 days)	To determine the potential of the test article to cause local effects	Pass
Subchronic Toxicity (90 days of subcutaneous implantation)	To evaluate the potential of the test article to cause local effects or subchronic/chronic systemic toxicity	Pass
Hemolysis	To assess the potential hemolytic activity of the test article in direct and indirect contact with rabbit blood	Pass
Complement Activation (C3a & SC5b-9)	To determine the potential complement activation in human plasma caused by the test article	Pass
<i>In vivo</i> Thrombogenicity	To evaluate safety of the test article and confirm the absence of abnormal thrombosis	Pass
Genotoxicity – Bacterial Reverse Mutation Assay	To evaluate the potential of the test article extracts to induce gene mutations	Pass
Genotoxicity – Mouse Lymphoma Assay	To evaluate the potential of the test article extracts to induce mutations (gene mutations and chromosomal damage)	Pass
Genotoxicity – <i>In vivo</i> Micronucleus Assay	To evaluate the potential of the test article extracts to induce clastogenic effects	Pass
Ion-Release	To evaluate the ion release of the test article after immersion at physiological conditions	Pass
Carcinogenicity	Leveraged from chemical characterization (not conducted)	Pass

The tests summarized in **Table 5** were performed to support the PKE delivery system as recommended for externally communicating devices contacting the circulating blood with limited exposure of < 24 hours.

Table 5: Delivery System Biocompatibility Testing

Test Performed	Test Purpose	Results
Cytotoxicity	To determine potential for cytotoxicity of the test article extract	Pass
Sensitization (Magnusson/Kligman)	To evaluate the allergenic potential or potential for sensitization of the test article extracts	Pass
Irritation/Intracutaneous Reactivity	To screen test article extracts for potential to produce irritation	Pass
Acute Systemic Toxicity	To screen test article extracts for potential systemic toxic effects	Pass
Pyrogenicity	To evaluate the potential of the test article extract to produce a pyrogenic response	Pass
Hemolysis	To assess the potential hemolytic activity of the test article in direct and indirect contact with rabbit blood	Pass
Complement Activation (C3a & SC5b-9)	To determine the potential complement activation in human plasma caused by the test article	Pass
<i>In vivo</i> Thrombogenicity	To evaluate the potential thrombogenicity of the test article	Pass
Genotoxicity – Bacterial Reverse Mutation Assay	To evaluate the potential of the test article extracts to induce gene mutations	Pass
Genotoxicity – Mouse Lymphoma Assay	To evaluate the potential of the test article extracts to induce mutations (gene mutations and chromosomal damage)	Pass
Genotoxicity – <i>In vivo</i> Micronucleus Assay	To evaluate the potential of the test article extracts to induce clastogenic effects	Pass

C. Sterilization

The PKE Stent System is sterilized with ethylene oxide (EO) gas to a sterility assurance level (SAL) of 1×10^{-6} in compliance with ISO 11135-1:2007 – *Sterilization of health care products -- Ethylene oxide -- Part 1: Requirements for development, validation and routine control of a sterilization process for medical devices*. The product has also been shown to meet the endotoxin limit of 20 EU/device in compliance with ANSI/AAMI ST72:2011 *Bacterial Endotoxins – Test methods, routine monitoring, and alternatives to batch testing*.

D. Packaging and Product Shelf-Life

Packaging verification testing was performed to demonstrate that the design of the PKE Stent System packaging can withstand the hazards of the distribution environment and that the sterility of the device is maintained throughout the labeled shelf-life. One year shelf-life was verified by conducting performance testing on samples that had been aged for one year.

E. Animal Studies

The purpose of the animal studies was to evaluate safety of the PKE Stent System under *in vivo* conditions at different time-points. Single and overlapped studies were conducted in porcine models. The single stent study examined the vascular response (e.g., amount of intimal area, degree of inflammation, thrombosis) of single implanted stents in comparison to two control devices: PKE Stent Systems without proBIO coating and Abbott Vascular Inc's MULTI-LINK VISION[®] stent (P020047, approved July 16, 2003) at 28 days.

The overlapping stent study (including a 28-day and 90-day follow-up time point) was conducted in healthy swine and evaluated the vascular response, including arterial late lumen loss and percent stenosis. Abbott MULTI-LINK VISION was used as the control. In addition, the delivery system was analyzed in order to evaluate relative thromboresistance of the materials *in vivo*. After 90 days, an analysis of downstream organs was conducted on the sacrificed animals. No concerning particulates or thrombi were observed.

All reported studies were conducted using healthy swine and were performed in accordance with the Good Laboratory Practice (GLP) for Non-clinical Laboratory Studies requirements outlined in 21 CFR Part 58 (Good Laboratory Practices). The results of the animal studies support the safety and performance of the device. A description of the studies and results is provided in **Table 6**.

Table 6: Summary of Animal Studies Conducted on the PKE Stent System

Study Type	Number of Animals	Implant Location	Testing Summary
28-day single stent study	N=14	LAD ¹ , LCX ² , RCA ³	At 28 days, angiographic parameters of stenosis (i.e.; percent diameter stenosis, minimal lumen diameter, late lumen loss) and histomorphometric parameters of stenosis (i.e.; intimal area, luminal area, area stenosis) were evaluated. While PKE showed slightly more favorable results, no significant difference was observed among the three groups for any of these parameters. Histopathology evaluation results showed significantly higher inflammation in Multi-Link Vision group than in the PKE with proBIO group. No other significant difference was present. The PKE with proBIO stents showed a reasonable safety profile without evidence of significant adverse effects.
28-Day interim follow-up of overlap stent study	N=8	LAD, LCX, RCA	All animals survived through 28 days. Angiography analyses showed statistically significantly greater late lumen loss and late loss index in the Multi-Link Vision group. No evidence of aneurysms, dissections, stent migration or thrombosis was observed. PKE stents showed a reasonable safety profile, without evidence of significant adverse effects.
90-Day final follow-up of overlap stent study	N=8	LAD, LCX, RCA	The stents of the 28-day interim animal study remained implanted through 90 days. Single stented sections were compared to overlapping sections for both groups. All stent pairs were systematically analyzed with regard to strut breakages. Injury score and neointimal immaturity score were significantly lower for PKE stents in overlapped and single stent segments. Intimal area, percent stenosis, and mean intimal thickness were significantly lower for PKE stents in single stent segments. In the overlapped stents, intimal area results were significantly lower for PKE stents. PKE stents showed a reasonable safety profile, without evidence of significant adverse effects.

¹Left Anterior Descending Artery; ²Left Circumflex Artery; ³Right Coronary Artery

X. SUMMARY OF PRIMARY CLINICAL STUDY

The applicant performed a clinical study to establish a reasonable assurance of safety and effectiveness of improving coronary luminal diameter in patients with de novo or restenotic lesions in native coronary arteries with a reference vessel diameter ranging from 2.25 mm to 4.0 mm and lesion length ≤ 31 mm with the PKE Stent System in the US under IDE #G110147. Data from this clinical study were the basis for the PMA approval decision. A summary of the clinical study is presented below.

A. Study Design

The BIOHELIX-I study was a prospective, non-randomized, multi-center, Investigational Device Exemption (IDE) study designed to demonstrate the safety and effectiveness of BIOTRONIK's PRO-Kinetic Energy Cobalt Chromium (CoCr) Coronary Stent System in subjects with atherosclerotic disease of native coronary arteries.

In total, BIOHELIX-I included 329 evaluable subjects at 33 study sites located across the United States, Europe and South America in order to evaluate the primary endpoint of the study. Study sites were required to be experienced in the placement of stents in the coronary arteries in order to qualify for enrollment into the study.

Patients were considered eligible for PRO-Kinetic Energy Cobalt Chromium (CoCr) Coronary Stent implantation if they had a de novo or restenotic lesion in a native coronary artery; restenotic lesions must have been previously treated with only standard PTCA (treatment must be > 12 months prior to the index procedure). Target lesions had to be in a major coronary artery (target vessel). The target vessels included the entire territory of the left anterior descending artery, left circumflex artery or right coronary artery and any major side branch of the artery. A maximum of one target lesion and one non-target lesion could be treated per subject. The lesions had to be located in separate coronary arteries, with treatment of the non-target lesion occurring first using commercially available therapy (with the exception of brachytherapy). Evaluable subjects were subjects that underwent an investigational stent implant procedure, which was defined as the stent system entering the guide catheter, regardless of whether the stent was successfully deployed.

The study utilized an independent angiographic core laboratory and an independent clinical events committee (CEC) to evaluate and adjudicate study primary endpoint data. The core laboratories and CEC were composed of experts in their field.

A1. Clinical and Angiographic Inclusion and Exclusion Criteria

Enrollment in the BIOHELIX-I study was limited to patients who met the following clinical and angiographic inclusion criteria in **Table 7**.

Table 7: Inclusion Criteria, BIOHELIX-I

Clinical Inclusion Criteria	• Age ≥ 18 years. • Willingness to comply with study follow-up requirements. • Candidate for a PCI procedure. • Candidate for coronary artery bypass graft surgery. • Documented evidence of stable or unstable angina pectoris or positive functional ischemia study (e.g. exercise treadmill test, thallium stress test, SPECT, stress echocardiogram or cardiac CT). – Stable angina pectoris is defined as a documented Canadian Cardiovascular Society Classification of I, II, III or IV. – Unstable angina pectoris is defined as a documented Braunwald Classification of B & C, I, II, III. • Written informed consent.
Angiographic Inclusion Criteria	• De novo or restenotic lesion in a native coronary artery; restenotic lesions must have been previously treated with only standard PTCA (treatment must have occurred > 12 months prior to the index procedure). • Target lesion must be in a major coronary artery (target vessel). The target vessel includes the entire territory of the left anterior descending artery, left circumflex artery or right coronary artery and any major side branch of the artery. • A maximum of one target lesion and one non-target lesion may be treated per subject. The lesions must be located in separate coronary arteries, with treatment of the non-target lesion occurring first using commercially available therapy (with exception of brachytherapy). • Lesions may be one solid lesion or a series of multiple, smaller lesions to be treated as one lesion. • Target lesion must be treatable with a single investigational stent; an additional stent may be used when treating a vessel dissection or another similar intra-procedure complication (use of investigational stent preferred). • Angiographic evidence of $\geq 50\%$ and $< 100\%$ stenosis (by operator visual estimate) with a TIMI flow > 1. • Target lesion length of ≤ 31 mm by operator visual estimate. • Target vessel reference diameter of 2.25 mm to 4.0 mm by operator visual estimate.

Patients were not permitted to enroll in the BIOHELIX-I study if they met any of the following exclusion criteria in **Table 8**.

Table 8: Exclusion Criteria, BIOHELIX-I

Clinical Exclusion Criteria	• Baseline LVEF of < 30%; LVEF may be measured and assessed by standard-of-care echocardiography procedures within 90 days of the index procedure or by a left ventriculogram prior to the index procedure (operator visual assessment). • PCI in any vessel 30 days prior to the index procedure or planned for within 30 days after the index procedure. • Stroke or transient ischemic attack within the last 6 months prior to enrollment. • Intolerance to contrast agents that cannot be medically managed and/or intolerance to antiplatelet, anticoagulant or thrombolytic medications. • Refusal of blood transfusions. • Any other medical condition that in the opinion of the investigator, poses an unacceptable risk for implant of a stent according to the study indications. • Pregnant, planning to become pregnant or nursing during the course of the study. Women of child-bearing potential must have a negative blood pregnancy (beta hCG) test. Female subjects who are surgically sterile or post-menopausal are exempt from having a pregnancy test. • Known allergy to L-605 CoCr alloy (cobalt, chromium, tungsten and nickel) or amorphous silicon carbide. • Life expectancy of less than one year. • Participation in any other clinical investigational device or drug study. Subjects may be concurrently enrolled in a post-market study, as long as the post-market study device, drug or protocol does not interfere with the investigational treatment or protocol of this study.
Angiographic Exclusion Criteria (visual estimate)	• Documented diagnosis of an acute MI within 72 hours of the index procedure and an elevation of Troponin or CKMB above the URL (CKMB measurement is not required if CK is normal) at the time of the index procedure (99th percentile of the individual investigative site's normal reference population). – For subjects with stable angina and elevated Troponin, CKMB <99% URL is required. • ECG changes consistent with an acute MI within 72 hours of the index procedure. ECG changes consistent with an acute MI include: – > 1 mm ST segment elevation or depression in consecutive leads – New LBBB. – Development of pathological Q-waves in two contiguous leads of the ECG. • Acute coronary syndrome with baseline Troponin > 99% URL. • INR $\geq$ 1.6. • Concomitant renal failure with serum creatinine level > 2.5 mg/dL. • Unresolved neutropenia (white blood cell count < 3,000 / μL), thrombocytopenia (platelet count < 100,000 / μL) or thrombocytosis (platelet count > 700,000 / μL). • Unprotected left main CAD (> 50% diameter stenosis by operator visual estimate). • Target vessel has been treated with any PCI procedure (e.g. PTCA, stent, cutting balloon, atherectomy, etc.) within 12 months prior to the index procedure. • Target lesion has been treated with a stent, cutting balloon or atherectomy any time prior to the index procedure or has been treated with PTCA within 12 months prior to the index procedure. • Target vessel treated with brachytherapy any time prior to index procedure.

	• Planned PCI in the target vessel within 9 months after the index procedure. • Target vessel has a non-target lesion with a > 50% stenosis that requires treatment during the index procedure. • Lesions preventing distal perfusion (TIMI flow 0 and 1) prior to wire crossing. • Target lesion is in the left main coronary artery or within 2 mm of the origin of the left anterior descending artery or left circumflex artery by operator visual estimate. • Target lesion is located within a saphenous vein graft or arterial graft. • Target lesion involves a bifurcation – lesion is located in a major coronary artery and involves a side branch with a diameter > 2 mm (by operator visual estimate). • Presence of a complication following pre-dilatation of target lesion. • Presence of a complication following treatment of a non-target lesion (if applicable). • Presence of a target vessel/lesion that has excessive tortuosity/angulation or is severely calcified preventing complete inflation of an angioplasty balloon. • Angiographic evidence of thrombus within the target lesion. • Target lesion is located within an aneurysm or associated with an aneurysm in the vessel segment either proximal or distal to the target lesion. • Use of cutting balloons, atherectomy or ablative devices immediately prior to investigational stent placement.
--	---

A2. Follow-up Schedule, BIOHELIX-I

All patients were scheduled to return for follow-up examinations at 30 days, 9, 12, 24 and 36 months post-index procedure. An ECG was required at the 9-month visit. Subjects were to receive 1 month of dual antiplatelet therapy and concurrent acetylsalicylic acid indefinitely. The study primary endpoint follow-up was completed on September 16, 2015 after all evaluable subjects completed a 9-month follow-up visit.

B. Study Endpoints

B1. Primary Endpoint

The primary endpoint for the BIOHELIX-I study was target vessel failure (TVF) rate at 9 months post- index procedure. Target vessel failure is defined as cardiac death, myocardial infarction (MI) and ischemia-driven target vessel revascularization (TVR). The TVF rate was compared with a performance goal established from a literature review of recent studies in a similar subject population.

The primary endpoint, TVF, was evaluated on an intent-to-treat basis, using the following design criteria:

- Test basis: exact test for one binomial population
- Type I error (alpha): 0.025 (one-sided)
- Statistical power: 80%
- Performance goal: 18.7%
- Expected TVF rate: 12.7%

A Kaplan Meier survival analysis was also performed as a supporting analysis to evaluate

the time to first failure for all subjects in the intent-to-treat (ITT) population.

B2. Secondary Endpoints

Secondary endpoints were not tested with formal hypotheses and only reported with descriptive statistics, including estimated rates and the associated exact, two-sided 95% confidence intervals. Event rates were estimated for the following endpoints at 30 days, 9, 12, 24 and 36-months post-index procedure unless otherwise noted:

- TVF rate (primary endpoint at 9 months)
- Individual components of the TVF rate (cardiac death, MI, ischemia-driven TVR)
- Overall TVR rate
- Target Lesion Failure (TLF) rate, including individual components of the TLF rate (cardiac death, MI, ischemia-driven Target Lesion Revascularization (TLR))
- Overall TLR rate
- Rate of all-cause mortality and all cause MI, including individual components
- Stent thrombosis rate
- Index procedure success
- Device success
- Lesion success
- Angina pectoris classification
- Rates for individual adverse events

B3. Exploratory Analyses

In addition to the secondary endpoint assessments, pre-specified covariates were examined to determine potential relationships with the primary study endpoint or its components.

Additional exploratory analyses of the primary endpoint were performed for the following subgroups:

- Patients with and without diabetes mellitus
- Small implanted stent diameter (≤ 2.75 mm) versus other stent diameters
- Long implanted stent length (≥ 30 mm) versus other stent lengths
- Treatment of a non-target lesion in addition to a target lesion versus treatment of a target lesion only
- Age ≤ 75 year versus age > 75 years

C. Accountability of PMA Cohort

At the time of database lock, of the 329 patients enrolled in the PMA study (intent to treat population), 97.3% (320/329) patients were available for the 9-month primary endpoint (five subject deaths, three subjects withdrew consent, and one subject was lost to follow-up).

Four of the patients that were exited prior to 300 days post-index procedure had primary endpoint events prior to exit and were included in the analysis population. Of the 320

patients available for 9-month evaluation, 308 subjects completed a 9-month study visit. Twelve subjects missed the 9-month evaluation; however six of these subjects returned at 12-months without an event and were included in the primary endpoint analysis. Of the six remaining subjects that did not return for a 9-month or 12-month visit, there were two that had an event prior to 9-months that were included in the primary endpoint analysis and four that were not included in the analysis population due to missing visit data.

D. Study Population Demographics and Baseline Parameters

Table 9 and **Table 10** present the baseline demographics and baseline risk factors respectively for the ITT population (N=329) at the time of the enrollment/baseline visit. The demographics of the study population are typical for a coronary stent study performed in the US.

Table 9: Baseline Demographics, ITT population (N=329)

Parameter	Evaluable
Age in years at enrollment	N = 329
Mean $\pm$ SD	69.0 $\pm$ 9.3
Range	35.7 to 89.0
Gender	N = 329
Male	226 68.7%
Female	103 31.3%
Race	N = 329
White	305 92.7%
Black or African American	17 5.2%
Asian	6 1.8%
American Indian or Alaska Native	1 0.3%
Native Hawaiian or other Pacific Islander	0 0.0%
Hispanic Ethnicity	N = 329
Hispanic or Latino	23 7.0%
Non-hispanic or non-Latino	306 93.0%

Table 10: Baseline Medical History, ITT population (N=329)

Category	Evaluable	
	N= 329	
Diabetes	94	28.6%
Diet controlled only	5	1.5%
Non-insulin medications	47	14.3%
Insulin with or without other medications	37	11.2%

Category	Evaluable	
	N=	329
No Treatment Reported	5	1.5%
Hypertension	275	83.6%
Hyperlipidemia	240	72.9%
Smoking status		
Current	60	18.2%
Within last 5 years	31	9.4%
Never/not within last 5 years	238	72.3%
History of myocardial infarction	67	20.4%
Prior CABG	27	8.2%
Prior percutaneous coronary revascularization	100	30.4%
Renal insufficiency	8	2.4%
LVEF, site reported	N = 322	
mean $\pm$ SD	56.9 $\pm$	8.1
range	30 to	90

E. Safety and Effectiveness Results

1. Safety Results

The primary endpoint of target vessel failure [TVF; defined as a composite of cardiac death, myocardial infarction (MI), and target vessel revascularization (TVR)] at 9-months post-index procedure in the ITT population was met and is shown below in **Table 11**. Note that cardiac death and MI are the safety components of the composite primary endpoint of TVF. The observed rate of TVF at 9-months was 9.06% (29/320, 95% CI: 6.15%, 12.76%) for the intent-to-treat (ITT) population. The observed rate was below the expected rate of 12.7%, and the null hypothesis that the TVF rate at 9 months is greater than or equal to the pre-specified Performance Goal of 18.7% was rejected ($p < 0.001$). The Per Protocol (PP) population with 9-month evaluations had a TVF rate of 8.28% (25/302, 95% CI: 5.43%, 11.98%).

The observed TVF rate supports the safety of the PRO-Kinetic Energy Cobalt Chromium (CoCr) Coronary Stent System in treating coronary atherosclerotic lesions and is comparable to TVF event rates reported for other recent coronary bare metal stent trials.

Table 11: Primary Endpoint, TVF Rate at 9 Months

Category	9 Months (300 days) Rate (%) [95% CI]
Intent-to-Treat Analysis (Primary)	n = 320
TVF¹	9.06% (29/320) [6.15%, 12.76%]
- Cardiac death	0.95% (3/317) [0.20%, 2.74%]
- MI	1.58% (5/316) [0.52%, 3.65%]
- Ischemia-driven TVR	7.26% (23/317) [4.65%, 10.69%]

¹Two patients experienced more than one mechanism of TVF therefore the composite rate of unique subjects is not equivalent to the sum of the components.

The analysis of safety and effectiveness was based on the ITT cohort of 329 patients. Key secondary endpoints related to safety are presented in **Table 12**. Key secondary endpoints related to effectiveness are also included in **Table 12** and are discussed in the next section.

- Individual components of the TVF composite rates of cardiac death, myocardial infarction and ischemia-driven TVR at 9 months were 0.95%, 1.58% and 7.26%, respectively in the ITT population.
- The overall definite/probable rate of stent thrombosis according to ARC definitions was 1.26% (4/318) at 9 months for the ITT population.
- Acute procedural success was achieved in 98.8% (325/329) of the ITT subjects. Device success and lesion success were both achieved in 99.4% (327/329) of the ITT subjects.
- Stable angina was reduced from 61.4% (202/329) at baseline to 11.0% (34/308) at 9 months post index procedure. Unstable angina was reduced from 11.9% (39/329) at baseline to 0.0% (0/308) at 9 months.

Table 12: Safety and Effectiveness Endpoints – ITT Population

Parameter	BIOHELIX-I, ITT Population
TVR at 9 months	7.89% (25/317) [5.17%, 11.42%]
Ischemia-driven TVR	7.26% (23/317)
Non-ischemia-driven TVR	0.96% (3/314)
TLF at 9 months	8.44% (27/320) [5.63%, 12.04%]
Cardiac death	0.95% (3/317)
MI	1.58% (5/316)
Ischemia-driven TLR	6.62% (21/317)
TLR at 9 months	7.26% (23/317) [4.65%, 10.69%]

Parameter	BIOHELIX-I, ITT Population
Ischemia-driven TLR	6.62% (21/317)
Non-ischemia-driven TLR	0.64% (2/314)
All-cause mortality/MI at 9 months	3.13% (10/320) [1.51%, 5.67%]
All-cause mortality	1.88% (6/319)
Cardiac	0.95% (3/317)
Non-cardiac	0.96% (3/313)
All-cause MI	1.58% (5/316)
Stent thrombosis at 9 months	
Definite	0.94% (3/318)
Probable	0.31% (1/318)
Total Definite/Probable	1.26% (4/318)
Possible	0.94% (3/318)
Stent thrombosis Timing – Definite/Probable at 9 months	
Acute (0-24 hours)	0.00% (0/318)
Subacute (>24 hours to 30 days)	0.31% (1/318)
Late (>30 days to 1 year)	0.94% (3/318)
Total Definite/Probable Stent thrombosis	1.26% (4/318)
Acute procedural success	98.8% (325/329)
Device success	99.4% (327/329)
Lesion success	99.4% (327/329)
Angina Pectoris Classification at 9 months	
No Angina	89.0% (274/308)
Stable Angina	11.0% (34/308)
Class I	6.2% (19/308)
Class II	2.9% (9/308)
Class III	1.3% (4/308)
Class IV	0.6% (2/308)
Unstable Angina	0.0% (0/308)

Adverse effects that occurred in the PMA clinical study:

No UADE's have been reported during the course of the BIOHELIX-I study. There have been 1229 adverse events, including 429 serious adverse events reported at the time of the database lock. **Table 13** presents the major clinical events that were observed in the ITT population that were serious and adjudicated by the Clinical Events Committee at the time of data analysis. This represents events reported for patients with a mean study follow-up duration of 1.8 ± 0.6 years/ patient.

Table 13: Summary of Major Clinical Events – Study Duration

Category	Rate % (n/329)
Deaths	3.95% (13/329)
Cardiac	1.22% (4/329)
Non-cardiac	2.74% (9/329)
Myocardial infarction events	0.91% (3/329)
Spontaneous MI, Q-wave	0.61% (2/329)
Spontaneous MI, Non Q-wave	0.30% (1/329)
Revascularization events	10.64% (35/329)
TLR	7.90% (26/329)
Ischemia-driven	7.29% (24/329)
Non-ischemia-driven	0.61% (2/329)
Non-TLR TVR	2.74% (9/329)
Ischemia-driven	2.13% (7/329)
Non-ischemia-driven	0.61% (2/329)
Stent thrombosis events, Definite/Probable	1.22% (4/329)
Definite, Subacute	0.30% (1/329)
Definite, Late	0.61% (2/329)
Probable, Late	0.30% (1/329)

The frequency and nature of adverse events observed in the BIOHELIX-I trial were similar to those observed for other bare metal stents approved in the United States.

2. Effectiveness Results

The analysis of effectiveness was based on the 329 evaluable patients at the 9-month time point. Key effectiveness outcomes are presented in **Tables 11 and 12**. The 9-month primary endpoint of TVF is a composite of safety and effectiveness endpoints, and the secondary endpoint analysis included both safety and effectiveness outcomes. The key effectiveness outcomes were Angina, All Revascularization, Ischemia-Driven TVR, and Ischemia-Driven TLR at 9-months. The effectiveness outcomes event rates are similar to those observed for other bare metal stents approved in the United States.

3. Subgroup Analyses

The following preoperative characteristics were evaluated for potential association with outcomes:

- The heterogeneity of the primary endpoint between males and females was tested by comparing the TVF rate between genders with a Fisher's Exact Test. An unadjusted p-value of 0.15 or less would have been considered evidence of a possible gender difference. There was no evidence ($p = 1.000$) of an association between the primary endpoint and Gender. The lack of an observed gender effect for the primary endpoint was also confirmed for the secondary endpoints analyzed.
- Pre-specified subgroups were examined to determine potential relationships with the primary study endpoint. The TVR rate at 9-months was analyzed in patients with diabetes (12.4%, 11/89), in patients with small implanted stent diameters ($\leq 2.75\text{mm}$) (12.1%, 14/116) and in patients > 75 years old (10.0%, 9/90). There were no significant differences in the TVR rate at 9 months for any of the subgroups analyzed.

4. Pediatric Extrapolation

In this premarket application, existing clinical data was not leveraged to support approval of a pediatric patient population.

F. Financial Disclosure

The Financial Disclosure by Clinical Investigators regulation (21 CFR 54) requires applicants who submit a marketing application to include certain information concerning the compensation to, and financial interests and arrangement of, any clinical investigator conducting clinical studies covered by the regulation. The pivotal clinical study included 235 investigators of which none were full-time or part-time employees of the sponsor and five had disclosable financial interests/arrangements as defined in 21 CFR 54.2(a), (b), (c) and (f) and described below:

- Compensation to the investigator for conducting the study where the value could be influenced by the outcome of the study: 0
- Significant payment of other sorts: 5
- Proprietary interest in the product tested held by the investigator: 0
- Significant equity interest held by investigator in sponsor of covered study: 0

The applicant has adequately disclosed the financial interest/arrangements with clinical investigators. Statistical analyses were conducted by FDA to determine whether the financial interests/arrangements had any impact on the clinical study outcome. The information provided does not raise any questions about the reliability of the data.

XI. PANEL MEETING RECOMMENDATION AND FDA’S POST-PANEL ACTION

In accordance with the provisions of section 515(c)(3) of the act as amended by the Safe Medical Devices Act of 1990, this PMA was not referred to the Cardiovascular Devices Advisory Panel, an FDA advisory committee, for review and recommendation because the information in the PMA substantially duplicates information previously reviewed by this panel.

XII. CONCLUSIONS DRAWN FROM PRECLINICAL AND CLINICAL STUDIES

The principal safety and effectiveness information for the PRO-Kinetic Energy Cobalt Chromium (CoCr) Coronary Stent System is derived from preclinical studies and from the BIOHELIX-I clinical trial.

The risks of the device are based on non-clinical laboratory and animal studies as well as data collected in a clinical study conducted to support PMA approval as described above.

Non-clinical testing performed during the design and development of the PRO-Kinetic Energy Cobalt Chromium (CoCr) Coronary Stent System confirmed the product design characteristics, specifications, and intended use.

The *in vitro* engineering testing conducted on the stent and delivery system demonstrated that the performance characteristics met the product specifications.

The biocompatibility and *in vivo* animal testing demonstrated that the acute and chronic *in vivo* performance characteristics of the PRO-Kinetic Energy Cobalt Chromium (CoCr) Coronary Stent System provide reasonable assurance of safety and acceptability for clinical use.

The test results obtained from the sterilization testing demonstrated that the product can be adequately sterilized and is acceptable for clinical use.

The shelf life testing has established acceptable performance for the labeled shelf life of one year.

A. Effectiveness Conclusions

The BIOHELIX-I multi-center clinical study evaluated the safety and effectiveness of the Pro-Kinetic Energy Cobalt Chromium (CoCr) Coronary Stent System in the treatment of atherosclerotic lesions in coronary arteries. The primary endpoint of the study was Target Vessel Failure (TVF, a composite of safety and effectiveness) at 9-months post-index procedure. The observed rate of TVF at 9-months was 9.06% (95% CI: 6.15%, 12.76%) for the intent-to-treat (ITT) population. The observed rate was below the expected rate of 12.7% and the null hypothesis that the TVF rate at 9 months is greater than or equal to the pre-specified Performance Goal of 18.7% was rejected ($p < 0.001$). Therefore, the primary endpoint of the BIOHELIX-I study was met.

The secondary endpoint analysis also evaluated effectiveness outcomes. The key effectiveness outcomes were Angina, All Revascularization, Ischemia-Driven TVR, and Ischemia-Driven TLR at 9-months. The effectiveness outcomes event rates are similar to those observed for other bare metal stents approved in the United States and therefore secondary endpoints at 9-months support the safety and effectiveness of the PRO-Kinetic Energy Cobalt Chromium (CoCr) Coronary Stent System. Long term evaluations at 24 months and 36 months require additional data collection and analysis due to the small number of evaluations completed; however, available data trends towards supporting the long-term effectiveness.

The data received and analyzed sufficiently demonstrates and supports the clinical safety and effectiveness of the PRO-Kinetic Energy Cobalt Chromium (CoCr) Coronary Stent System in the treatment of atherosclerotic lesions in coronary arteries. The data also provides evidence that the safety and effectiveness results are similar for important sub-groups, including female, elderly, and diabetic patients.

B. Safety Conclusions

As noted above, the primary endpoint of the BIOHELIX-I study was met, and the study satisfactorily demonstrated the safety of the PRO-Kinetic Energy Cobalt Chromium (CoCr) Coronary Stent System. Individual components of the TVF composite rates of cardiac death, myocardial infarction and ischemia-driven TVR at 9 months were 0.95%, 1.58% and 7.26%, respectively in the ITT population. The overall definite/probable rate of stent thrombosis according to ARC definitions was 1.26% (4/318) at 9 months for the ITT population. There have been 429 serious adverse events reported in 153 evaluable subjects, and 190 adverse events reported as device- and/or procedure-related in 118 evaluable subjects. The percentage of evaluable subjects with a serious adverse event is 46.5% and the percentage of evaluable subjects with a device- and/or procedure-related adverse event is 35.9%. Long term evaluations at 24 months and 36 months require additional data collection and analysis due to the small number of evaluations completed; however, available data trends towards supporting the long-term safety.

No UADEs occurred during the BIOHELIX-I study and the overall adverse event profile and frequency of events observed was similar to those previously observed for approved bare metal stents.

C. Benefit-Risk Determination

The probable benefits of the Pro-Kinetic Energy Cobalt Chromium (CoCr) Coronary Stent System are also based on data collected in the clinical study conducted in support of PMA approval as described above. The results of the BIOHELIX-I study demonstrated positive clinical outcomes:

- Rates of TVF and TVR events below the performance goal established from literature;

- Acceptably low rates of safety events, including stent thrombosis;
- Device success rate of 99.4%.

These benefits outweigh risks when used as intended according to the Instructions for Use, as determined by the product risk analysis. No new risks were identified in the BIOHELIX-I study and the overall risks were similar to those observed for other marketed bare metal stents.

Additional factors to be considered in determining probable risks and benefits for the PRO-Kinetic Energy Cobalt Chromium (CoCr) Coronary Stent System include the following:

- The study was designed based on prior IDE trials conducted in support of PMA approval for other coronary bare-metal stents. The primary endpoint results rejected the null hypothesis of the performance goal with a p-value less than 0.05.
- The study was conducted with similar methodologies as other coronary stent IDE clinical trials using comparable performance goals.
- The results of the study can be applied to the general population of patients with coronary artery disease. The study was conducted on a typical population of subjects with coronary artery disease. The study did not exclude any typical patient subgroups that would be expected to benefit from treatment.
- Risks are identifiable and similar to those previously reported and observed for other coronary balloon expandable cobalt chromium stents.
- There are several alternatives for the correction of coronary artery disease, which include: percutaneous transluminal angioplasty (PTA), stenting with another stent for which there is an approved indication, bypass surgery, lifestyle modifications, and medical therapy. When treatment beyond medications and lifestyle modification is warranted, patients often choose stent deployment over surgical revascularization because of the less invasive nature of this procedure and the more rapid recovery time associated with percutaneous coronary intervention.
- This submission did not include specific information on patient perspectives for this device.

In conclusion, given the available information above, the data support that for improving coronary luminal diameter in patients with de novo or restenotic lesions in native coronary arteries with a reference vessel diameter ranging from 2.25 mm to 4.0 mm and lesion length $\leq$ 31 mm, the probable benefits outweigh the probable risks.

D. Overall Conclusions

The data in this application support the reasonable assurance of safety and effectiveness of this device when used in accordance with the indications for use.

XIII. CDRH DECISION

CDRH issued an approval order on February 14, 2017. The final conditions of approval cited in the approval order are described below.

1. ODE Lead PMA Post-Approval Study – Extended Study of the Premarket Cohort (PRO-Kinetic Energy Cobalt Chromium (CoCr) Coronary Stent System BIOHELIX-I Study): The Office of Device Evaluation (ODE) will have the lead for this clinical study, which was initiated prior to device approval. The Extended Follow-up Study is a prospective, non-randomized, multi-center study which enrolled 329 subjects evaluable for the primary endpoint analyses. The primary endpoint of the BIOHELIX-I Study was target vessel failure [TVF; defined as a composite of cardiac death, myocardial infarction (MI), and target vessel revascularization (TVR)] evaluated at nine (9) months post-index procedure against a performance goal of 18.7%. The applicant will collect and report to the Agency clinical outcomes through 36 months post-index procedure on the 329 subjects enrolled in the BIOHELIX-I Study.

The applicant's manufacturing facilities have been inspected and found to be in compliance with the device Quality System (QS) regulation (21 CFR 820).

XIV. APPROVAL SPECIFICATIONS

Directions for use: See device labeling.

Hazards to Health from Use of the Device: See Indications, Contraindications, Warnings, Precautions, and Adverse Events in the device labeling.

Post-approval Requirements and Restrictions: See approval order.